IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NO: 09/992,235

FOR: (R,S'), (R,R')-AMPHETAMINIL, COMPOSITIONS AND USES THEREOF

DATE FILED: 11/06/2001

FIRST NAMED INVENTOR: SETH LEDERMAN

EXAMINER: ROYDS, LESLIE A.

ART UNIT: 1614

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF HERBERT HARRIS, M.D., Ph.D. UNDER 37 CFR 1.132

Sir:

I, Herbert Harris, M.D., Ph.D. hereby declare the following:

1. I am presently the Chief Medical and Scientific Officer for Krele Pharmaceuticals, Inc. with an office in Research Triangle Park, NC.

2. Among, my credentials, I received an M.M. and a Ph.D. in Pathology from the University of Pittsburgh School of Medicine and completed my medical residency at the Department of Psychiatry, Yale School of Medicine and I obtained my B.A. degree from Georgetown University College of Arts and Sciences. My Curriculum Vitae is attached hereto.

3. It is my understanding that claims 1-8, 30-31, 36 and 38 of the above-mentioned application are being rejected under 35 USC 103(a) as being

obvious in view of the Salvesen et al. reference in light of STN Registry File No. 17590-01-1 and Stedman's Medical Dictionary (Twenty-Second Edition, 1972; p.377) each cited to show facts, in view of Remington's Pharmaceutical Sciences (Sixteenth Edition, 1980; ppp.420-426).

4. Furthermore I understand that the Examiner agrees that at the dose of 1 mg/kg the claimed invention shows unexpected results which renders the claimed invention nonobvious.

5. In my statistical analysis of the results presented in the patent application I took the 95% confidence boundaries around the 1 mg/kg points from Figures 3A and 7A and projected them onto a regression line that fit the data. From this I was able to calculate the mg/kg values that corresponded to the upper and lower 95% confidence bands. It is my belief that when statistical analyses are performed on the data points of Figures 3A and 7A one can expect to observe the benefits of the claimed invention in the range of 0.8-1.3 mg/kg from the cumulative locomotor data (Figure 3C) and in the range of 0.7-1.4 mg/kg from the stereotypy data (Figure 7C).

6. The calculations I used to get the dose ranges were based solely on data in the application. The 1 mg/kg points are included in the Figures 3A and 7A that accompany the application. I used these points along with the error bars around them (also in the application) to construct confidence intervals and derive corresponding mg/kg doses.

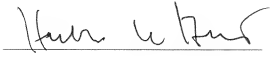
7. This was relatively easy for me because I have a computer program (GraphPad) which allowed me to "open" the figures and extract the numerical data underlying the points and error bars. However, the data was already present in the original application. A scientist could actually measure these numbers directly from the graphs.

8. Thus, it is my belief that the statistical analysis of the 1 mg/kg dose points in Figures 3A and 7A show that similar unexpected results would be obtained in the ranges of 0.8-1.3 mg/kg or 0.7-1.4 mg/kg.

9. Separately, it is my understanding that the Examiner believes that the unexpected results have only been demonstrated using 100% DMSO as a vehicle.

10. However, it is my knowledge and belief that DMSO is merely an inert diluent and in no way is affecting the unexpected results observed. DMSO is frequently used as a vehicle in preclinical studies and in no way is to restrict the use of other diluents used in clinical studies or medical treatments for purposes of the claimed invention.

11. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under article 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.



Herbert Harris

Chief Medical and Scientifc Officer

Krele Pharmaceuticals, Inc.

CURRICULUM VITAE FOR HERBERT HARRIS, M.D., PH.D.

2009-present: Chief Medical and Scientific Officer, Krele Pharmaceuticals, RTP, North Carolina

Professional Experience

2007-2009: Chief Medical Officer, Validus Pharmaceuticals, Parsippany, NJ

- Direct oversight of Clinical Development, Regulatory Affairs, Drug Safety, and Medical Affairs

2005-2007: Executive Director, Jazz Pharmaceuticals, Palo Alto, CA

- Therapeutic area head for psychiatry
- Phase I-III programs in fibromyalgia, epilepsy, GAD, bipolar disorder, panic disorder, schizophrenia, and primary insomnia
- NDA and commercial launch activities for Luvox CR

2003-2005: Clinical Associate Professor, Department of Psychiatry, University of North Carolina, Chapel Hill, Chapel Hill, NC

2003-2005: Senior Director, Psychiatry Medicine Development Center, GlaxoSmithKline, Research Triangle Park, NC

- Design and conduct of Phase II-IV clinical trials
- Member, Genetics Research Therapeutic Area Team for Psychiatry providing strategic direction for pharmacogenomics and molecular target identification

2001-2003: Chief Medical Officer, Vela Pharmaceuticals, Lawrenceville, NJ

- Chief physician responsible for medical monitoring and safety of clinical trials in all therapeutic areas including IBS, fibromyalgia, anorexia nervosa, depression
- Preclinical research resulting in multiple patents and IND fillings

2000-2001: Director, Clinical Operations, Worldwide Clinical and Regulatory

Affairs. Cephalon Inc. West Chester, PA

- Designed and implemented phase I-III clinical trials for Shift Work Sleep Disorder, Parkinson's disease, Generalized Anxiety Disorder, and amyotrophic lateral sclerosis

1999-2000: Associate Director, Clinical Psychopharmacology, Merck Research Laboratories, Blue Bell, PA

- Designed and implemented phase II, III clinical trials for depression

1996-1999: Chief, Geriatric Psychopharmacology and Geriatric Clinical Neurosciences Programs (DSIR); and Acting Chief, Adult Psychopathology, Behavior, and Prevention Branch (DAHBR), NIMH, Bethesda, MD

- Responsible for NIMH programmatic initiatives:
    - RFP NIMH-99-DS-0003: Treatment Resistant Depression (STAR*D)
    - TPA-99-010: Pilot Effectiveness Trials for Mental Disorders
    - TPA-99-011: NIMH Therapeutic Effectiveness Protocol Development Program
    - RFA: MH-97-003: Molecular Mechanisms of Mental Disorders of Late Life
- Responsible for r&d PROGRAMS ranging from $9-60 Million
- Contributed to the Surgeon General's Report on Mental Illness and DSM-IV (TR)

1997-1998 Visiting Scientist, Division of Neuropharmacological Products, Food and Drug Administration

- Scientific liaison between FDA and NIMH

1994-1996: Senior Staff Fellow, Laboratory of Neurosciences, NIA

- Investigated biochemical mechanisms of programmed cell death in Alzheimer's disease
- Developed a novel PCR techniques for identification of differentially expressed gene products

1993-1994: Postdoctoral Research, Laboratory of Molecular Psychiatry, Yale University School of Medicine

- Studied biochemical effects of chronic opiate and cocaine administration on signal transduction systems in the brain

Training and Education

1990-1994: Psychiatric Residency, Department of Psychiatry, Yale University School of Medicine, New Haven, CT.

1990: M.D., University of Pittsburgh School of Medicine, Pittsburgh, PA

1989: Ph.D., Department of Pathology, University of Pittsburgh School of Medicine, Pittsburgh, PA

1983: B.A., Philosophy, Georgetown University College of Arts and Sciences Washington, D.C.

Other Positions

Member, Cognition Working Group, OMERACT (Outcome Measures in Rheumatology) Working Group for Fibromyalgia (2007)

Member, Executive Committee, International Society for CNS Drug Development (2005-2007)

Medical Advisor, NIMH CATIE Study (2002-2003)

Grant Reviewer, Special Emphasis Panel, and SBIR Programs, NIMH (2002-2004)

Corresponding Member, Committee on Psychiatric Diagnosis and Assessment of the American Psychiatric Association (1999-2000)

Member, Committee of Black Psychiatrists of the American Psychiatric Association (1994-2000)

Board of Directors, Affiliated Community Counselors, a nonprofit organization providing mental health services in Maryland (1996-1997)

Medical Director of Psychiatric Services, Collingswood Nursing Home and Manor Care, Chevy Chase Nursing Home Dementia Unit, 1996-1999

Attending Psychiatrist: Charter Behavioral Health System, Rockville, MD

1995-1999 Potomac Valley Wellness Center, Rockville, MD Genesis ElderCare Nursing Home, Silver Spring, MD

National Lutheran Nursing Home, Rockville, MD

Licensure and Certification

1990 Diplomate, American Board of Medical Examiners

1994. Licensed Physician, State of Maryland # D45999

1997 Diplomate, American Board of Psychiatry and Neurology

1999 Licensed Physician, State of Pennsylvania # MD 070371-L

2010 Licensed Physician, North Carolina # 2010-00610

Professional Organizations

American Psychiatric Association

International Society for Drug Development

American Society for Experimental Neurotherapeutics

North Carolina Psychiatric Association